

**AMENDMENT AND RESPONSE TO OFFICE ACTION**

**Remarks**

Claim 1 has been amended to specify that the poly(ester-anhydride) comprises monomers derived from ricinoleic acid and sebacic acid. Support for the amendment is found at least in Examples 4 and 11-14 in the specification.

Claims 4-7 have been canceled.

Claims 11-14 were canceled in response to the restriction requirement. These claims were inadvertently included in the amendment and response filed on February 4, 2008. Claims 11-14 are marked as canceled in this amendment and response.

New dependent claim 15 was added. Support for the amendment is found at least in Examples 4 and 11-14 in the specification.

Applicants believe that it is proper for the present amendment to be entered since it places the application in condition for allowance. Alternatively, entry of this amendment is proper since it places the claims in better form for appeal, does not raise any new issues, and does not require further consideration or search. Additionally, by amending claims, the claimed subject matter is narrowed since it is limited to compositions comprising a poly(ester-anhydride) composed of monomers derived from ricinoleic acid and sebacic acid in a weight ratio of 7:3 or 8:2.

Applicants reserve the right to pursue claims of a broader scope in one or more continuation applications.

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**Rejection Under 35 U.S.C. § 112, first paragraph**

Claims 1-10 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner alleges that the limitation that the poly(ester-anhydride) contains random amide bonds is new matter. Without making any admissions and solely for the purpose of facilitating prosecution, claim 1 has been amended to delete this limitation.

**Rejection Under 35 U.S.C. § 112, second paragraph**

Claims 4-7 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner alleges that claims 4-7 are indefinite because claim 1 requires the presence of amide bonds in the polymer. However, the polyester anhydride structure shown in claim 4 does not have an amide bond because R' is ricinoleic acid and R" is an aliphatic or aromatic moiety. The Examiner is incorrect. Claim 1 does not require the presence of amide bonds as alleged by the Examiner, rather amide bonds are in the alternative. However, in order to facilitate prosecution and without making any admissions, claim 1 has been amended to delete the limitation regarding random amide bonds in the polymer backbone. Claims 4-7 have been deleted. Therefore, the Examiner's rejection is moot.

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**Rejection Under 35 U.S.C. § 102/103**

Claims 1 and 6-8 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,856,652 to Storey *et al.* ("Storey"). Claims 1 and 6-8 were rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 4,414,381 to Griffin *et al.* ("Griffin"). Claims 1-7 and 10 were rejected under 35 U.S.C. § 102(b) as being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Teomim *et al.*, *J. Biomed. Mat. Res.*, Vol. 45, Issue 3, 258-267 (1999) ("Teomim") or Domb *et al.*, *Acta Polymérica*, Vol. 49, Issue 10-11, 526-533 (Dec. 14, 1998) ("Domb"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

*The Legal Standard*

For a rejection of claims to be properly founded under 35 U.S.C. § 102, it must be established that a prior art reference discloses each and every element of the claims. *Hybritech Inc. v Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986), cert. denied, 480 US 947 (1987); *Scripps Clinic & Research Found v. Genentech Inc.*, 18 USPQ2d 1001 (Fed. Cir. 1991). The Federal Circuit held in Scripps, 18 USPQ2d at 1010:

Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. . . . *There must be no difference* between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. (Emphasis added)

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A reference that fails to disclose even one limitation will not be found to anticipate, even if the missing limitation could be discoverable through further experimentation. As the Federal Circuit held in Scripps, *Id.*:

[A] finding of anticipation requires that all aspects of the claimed invention were already described in a single reference: a finding that is not supportable if it is necessary to prove facts beyond those disclosed in the reference in order to meet the claim limitations. The role of extrinsic evidence is to educate the decision-maker to what the reference meant to persons of ordinary skill in the field of the invention, not to fill in the gaps in the reference.

For a prior art reference to anticipate a claim, it must enable a person skilled in the art to practice the invention. The Federal Circuit held that "a §102(b) reference must sufficiently describe the claimed invention to have placed the public in possession of it. . . [E]ven if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *Paperless Accounting Inc v Bay Area Rapid Transit Sys.*, 231 USPQ 649, 653 (Fed. Cir. 1986).

Analysis

Claim 1 has been amended to specify that the poly(ester-anhydride) is composed of monomers derived from ricinoleic acid and sebacic acid. Support for the amendment is found at least in Examples 4 and 11-14 in the specification.

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*Storey*

Storey describes biodegradable poly(ester-anhydrides) (abstract). Storey discloses that the polyester segment components can contain a homopolymer, copolymer, or terpolymer of biocompatible hydroxy acids, for example, lactic acid, glycolic acid,  $\epsilon$ -hydroxycaprylic acid and  $\gamma$ -hydroxyvaleric acid (col. 3, lines 27-31). Alternatively, Storey discloses, the polyester segments can be formed by copolymerization of a polyhydric alcohol and a biocompatible polycarboxylic acid (col. 3, lines 31-33). Storey discloses that most typically, such copolymers are formed between dihydric alcohols, for example, propylene glycol, and biocompatible dicarboxylic acids (col. 3, lines 33-36). Representative diacids include Kreb cycle intermediate such as citric, isocitric, cis-aconitic,  $\alpha$ -ketoglutaric, succinic, maleic, oxaloacetic, and fumaric acids (col. 3, lines 36-41). Storey does not disclose or suggest a poly(ester-anhydride) comprising monomers derived from ricinoleic acid and sebacic acid. Storey does not disclose or suggest a poly(ester-anhydride) comprising monomers derived from ricinoleic acid and sebacic acid suitable for administration by injection as required by claim 3 or having the weight ratio specified in claim 15. Storey does not disclose and every element of the claims. Accordingly, claims 1, 6-10, and 15, as amended, are novel over Storey.

*Griffin*

Griffin describes a melt processable aromatic poly(ester-anhydride) (abstract). In contrast, the claims, as amended, specify that the poly(ester-anhydride) comprises monomers derived from ricinoleic acid and sebacic acid, which are aliphatic molecules, not aromatic

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molecules. Griffin does not disclose or suggest poly(ester-anhydrides) prepared from ricinoleic acid and sebacic acid. Griffin does not disclose or suggest poly(ester-anhydrides) prepared from ricinoleic acid and sebacic acid suitable for administration by injection as required by claim 3 or having the weight ratio defined in claim 15. Griffin does not disclose each and every element of the claims. Accordingly, claim 1, 6-10, and 15, as amended, are novel over Griffin.

***Teomim***

Teomim describes polyanhydrides synthesized from ricinoleic acid half-esters with maleic and succinic anhydrides (abstract). The polymers described in Teomim are polyanhydride copolymers that are formed from the melt condensation of diacids and contain only anhydride bonds. Teomim does not disclose or suggest poly(ester-anhydrides), let alone poly(ester-anhydrides) comprising monomers derived from ricinoleic acid and sebacic acid as required by claim 1. Teomim does not disclose or suggest poly(ester-anhydrides) comprising monomers derived from ricinoleic acid and sebacic acid having the weight ratio specified in claim 15. Teomim does not disclose or suggest each and every element of the claims. Accordingly, claims 1, 7-10, and 15, as amended, are novel over Teomim.

Further, one of ordinary skill in the art would not be motivated to modify the polyanhydrides of Teomim to arrive at the claimed composition. The claimed compositions contain a poly(ester-anhydride) comprising monomers derived from ricinoleic acid and sebacic acid. These polymers are liquids at room temperature (page 31, lines 12-14). These polymers release incorporated active agents over several weeks, which is longer than solid polymers

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prepared from the same monomers (page 7, lines 27-30). The slower release is due to the fact that when the polymer are placed in an aqueous medium (e.g., buffer solution, or tissue or biological mediums), the viscosity of the polymer increases (page 7, line 30 to page 8, line 3). This increase in viscosity results in a semisolid compact implant that keeps it integrity while slowly degrading and releasing incorporated drug (page 8, lines 3-6). These polymers also exhibited improved solubility compared to polyanhydrides (page 31, line 17 to page 32, line 2). The slower release of incorporated active agents and improved stability could not have been predicted from the polyanhydrides described in Teomim. Accordingly, claims 1, 7-10, and 15, as amended, are not obvious over Teomim.

***Domb***

Domb describes biopolymers for use as drug carriers and bioactive macromolecules (abstract). Domb discloses that polyanhydrides synthesized from non-linear hydrophobic fatty acid esters, based on ricinoleic acid, maleic acid, and sebacic acid allegedly possess desired physicochemical properties (page 526, 2<sup>nd</sup> column, 4<sup>th</sup> paragraph, lines 8-11). These polymers are polyanhydrides (i.e., contain only anhydride bonds), not poly(ester-anhydrides).

Domb also discloses block copolyester-anhydrides (page 530, 1<sup>st</sup> col., 2<sup>nd</sup> paragraph). Domb describes ABA-type block copolymers of poly(propylene fumarate) (PPF) and lactide (page 530, 1<sup>st</sup> col., 3<sup>rd</sup> paragraph). The ester bonds in the block copolyester-polyanhydride polymers described in Domb are between the ester monomers units in the ester block (see structure 4 on page 530). In contrast, the polymers in the claimed compositions contain ester

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bonds between the ricinoleic acid and sebacic acid monomer units. Domb does not disclose or suggest poly(ester-anhydrides) comprising monomers derived from ricinoleic acid and sebacic acid having the weight ratio specified in claim 15. The block copolyester-polyanhydrides have a weight ratio of 1:1 (*see structure 4 on page 530*). Domb does not disclose each and every element of the claims. Accordingly, claims 1, 7-10, and 15, as amended, are novel over Domb.

Further, one of ordinary skill in the art would not be motivated to modify the block copolyester-polyanhydrides of Domb to arrive at the claimed composition. The Examiner alleges that Domb is silent regarding the random nature of the ester bond in the block copolyester-anhydrides. The Examiner is incorrect. As discussed above, the copolyester-polyanhydrides described in Domb are block copolymers, wherein the ester bonds are between the monomer units in the ester block, not between monomers derived from ricinoleic acid and sebacic acid as required by the claims.

As discussed above, the polymers in the claimed compositions are liquids at room temperature and release incorporated active agents over several weeks, which is longer than solid polymers prepared from the same monomers (page 7, lines 27-30). The slower release is due to the fact that when the polymer are placed in an aqueous medium (e.g., buffer solution, or tissue or biological mediums), the viscosity of the polymer (page 7, line 30 to page 8, line 3). This increase in viscosity results in a semisolid compact implant that keeps it integrity while slowly degrading and releasing incorporated drug (page 8, lines 3-6). The polymers also exhibit improved stability compared to polyanhydrides (page 31, line 17 to page 32, line 2). In contrast,

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the block copolyester-polyanhydrides described in Domb are described as being rubber like. The ABA block copolymers and the anhydride polymers described in Domb were degraded *in vitro* within four weeks. The slower degradation times of the polymers in the claimed compositions could not have been predicted from the polyanhydrides and block copolyester-polyanhydrides described in Domb. Accordingly, claims 1, 7-10, and 15, as amended, are not obvious over Domb.

**Rejection Under 35 U.S.C. § 103**

Claims 1, 2, 3, 9, and 10 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Storey, in view of U.S. Patent No. 5,648,096 to Gander *et al.* ("Gander") or U.S. Patent No. 5,626,862 to Brem *et al.* ("Brem").

**Legal Standard**

Obviousness is a legal conclusion based on underlying facts of four general types, all of which must be considered by the examiner: (1) the scope and content of the prior art; (2) the level of ordinary skill in the art; (3) the differences between the claimed invention and the prior art; and (4) any objective indicia of nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459 (1966). This standard was recently affirmed by the Supreme Court in *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727, 82 U.S.P.Q.2d 1385 (2007). The Court did not totally reject the use of "teaching, suggestion, or motivation" as a factor in the obviousness analysis. Rather, the Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in

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determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a). The Supreme Court did not obviate the requirement for the references to provide some motivation to combine as applicants have done, with a reasonable expectation of success.

"Focusing on the obviousness of substitutions and differences, instead of on the invention as a whole, is a legally improper way to simplify the often difficult determination of obviousness." *Gillette Co. v. S.C. Johnson & Sons, Inc.*, 919 F.2d 720, 724, 16 U.S.P.Q.2d 1923 (Fed. Cir. 1990); *see Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383, 231 U.S.P.Q. 81, 93 (Fed. Cir. 1986). "One cannot use hindsight reconstruction to pick and choose among isolated disclosures on the prior art to deprecate the claimed invention." *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988).

Analysis

Claim 1 has been amended to specify that the poly(ester-anhydride) is composed of monomers derived from ricinoleic acid and sebacic acid in a weight ratio of 7:3 or 8:2. Support for the amendment is found at least in Examples 4 and 11-14 in the specification.

Storey in view of Gander or Brem

Storey is discussed above. Storey does not disclose or suggest a poly(ester-anhydride) comprising monomers derived from ricinoleic acid and sebacic acid. Storey does not disclose or suggest a poly(ester-anhydride) comprising monomers derived from ricinoleic acid and sebacic acid suitable for administration by injection as required by claim 3 or having the weight ratio specified in claim 15.

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Gander and Brem disclose microimplants, such as microparticles, microspheres, and microcapsules can be used to encapsulate and deliver drugs. Gander and Brem, alone or in combination, do not disclose or suggest a poly(ester-anhydride) comprising monomers derived from ricinoleic acid and sebamic acid as required by claim 1, suitable for administration by injection as required by claim 3, or having a weight ratio of 7:3 or 8:2 as required by claim 15. Gander and Brem do not cure the deficiencies of Storey. Accordingly, claims 1, 2, 3, 9, and 10 are not obvious over Storey in view of Gander or Brem.

Allowance of claims 1, 2, 3, 9, 10 and 15, as amended, is respectfully solicited.

Respectfully submitted,

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